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## TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

9

Application Number	10/805,099
Filing Date	March 19, 2004
First Named Inventor	Chunhui Xu, et al.
Art Unit	1632
Examiner Name	Thaian N. Ton
Attorney Docket Number	099/004P

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached  <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s)  <input type="checkbox"/> Extension of Time Request  <input type="checkbox"/> Express Abandonment Request  <input checked="" type="checkbox"/> Information Disclosure Statement (2 pages)  <input type="checkbox"/> Certified Copy of Priority Document(s)  <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers  <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address  <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund  <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please Identify below):
<input type="checkbox"/> Remarks  Form PTO-1449 (6 pages) with copies of 32 references		

### SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Geron Corporation		
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Printed name	Bart W. Wise		
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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: Chunhui Xu *et al.*

Art Unit: 1632

Serial No.: 10/805,099

Examiner: TBD

Filing Date: March 19, 2004

Attorney Docket: 099/004

For: PROCESS FOR MAKING TRANSPLANTABLE  
CARDIOMYOCYTES FROM HUMAN  
EMBRYONIC STEM CELLS

## INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97

Commissioner for Patents  
Arlington, VA 22313-1450

Dear Sir:

The information listed in the accompanying Form PTO-1449 and provided herewith may be material to examination of this application and is submitted in compliance with the duty of disclosure under 37 CFR § 1.56. The Examiner is requested to make this information of record in the application.

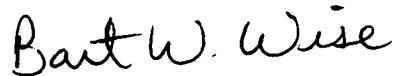
PATENT  
Serial No. 10/805,099  
Docket: 099/004  
Information Disclosure Statement

Serial No. 10/193,884, to which this application claims priority under 35 U.S.C. §120. This is in compliance with the provisions of 37 C.F.R. §1.98(d).

This Information Disclosure Statement is not to be construed as a representation that a full search for relevant information has been made, that all relevant information has been found, or that the information provided with this Statement is considered to be material to patentability of the claimed invention as defined under 37 CFR § 1.56(b).

It is believed that no fee is required for submission of this Statement, which is filed before the first Office Action on the merits of the application. Nevertheless, should a fee be required for consideration of this Statement and the listed information, the Assistant Commissioner is authorized to charge such fee to Deposit Account No. 07-1139, referencing the attorney Docket Number indicated above.

Respectfully submitted,



Bart W. Wise  
Registration No. 49,029

GERON CORPORATION  
230 Constitution Drive  
Menlo Park, CA 94025  
*Telephone: (650) 473-7753*  
*Fax: (650) 473-8654*

DATE: January 13, 2006

<p>Form 1449 (modified) 37 C.F.R. §1.97 Information Disclosure Statement By Applicant JAN 17 2006 (Use Several Sheets if Necessary)</p>				Docket: 099/004P Title: Process for Making Transplantable Cardiomyocytes from Human Embryonic Stem Cells Inventors: Chunhui Xu, et al. Filing Date: March 19, 2004	U.S.S.N. 10/805,099 Group: 1632
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### U.S. Patent Documents

Examiner Initial	Ref.	Patent No.	Filing Date	Publication Date	Class/ Subclass	Inventors	Title
/MN/	A	5,733,727	Jun 7/95	Mar 31/98	435/6	Field	Myocardial grafts and cellular compositions
	B	5,843,780	Jan 18/96	Dec 1/98	435/363	Thomson	Primate embryonic stem cells
	C	5,928,943	Nov 21/95	Jul 27/99	435/363	Franz, et al.	Embryonal cardiac muscle cells, their preparation and their use
	D	6,015,671	Nov 21/97	Jan 18/00	435/6	Field	Myocardial grafts and cellular compositions
	E	6,099,832	Jun 19/98	Aug 8/00	424/93.21	Mickle, et al.	Transplants for myocardial scars
	F	6,110,459	May 28/97	Aug 29/00	424/93.21	Mickle, et al.	Transplants for myocardial scars and methods and cellular preparations
	G	6,245,566	Mar 31/98	Jun 12/01	435/384	Gearhart, et al.	Human embryonic germ cell line and methods of use
	H	6,261,836	May 9/97	Jul 17/01	435/325	Cech, et al.	Telomerase
	I	6,387,369	Jul 14/98	May 14/02	424/93.7	Pittenger, et al.	Cardiac muscle regeneration using mesenchymal stem cells
	J	6,399,300	Nov 16/99	Jun 4/02	435/6	Field	Myocardial grafts and cellular compositions useful for same
	K	6,534,052	Sep 05/00	Mar 18/03	424/93.2	Xiao, et al.	Cardiac function comprising implantation of embryonic stem cell in which differentiation has been initiated
	L	US 20050037489	Jan 20/04	Feb 17/05	435/366	Gepstein, et al.	Methods of inducing differentiation of stem cells
/MN/	M	US20050227353	Jan. 14/04	Oct 13/05	435/366	Mummery	Methods of Inducing differentiation of stem cells

### Foreign Patent or Published Foreign Patent Application

Examiner Initial	Ref.	Document No.	Publication Date	Jurisdiction	Title	Translation
/MN/	N	AU 729377	Feb 1/01	Australia	Methods and materials for the growth of primate-derived primordial stem cells in feeder-free culture	N/A
	P	WO 92/13066	Aug 6/92	PCT	Mammalian cardiac myocyte cell line	N/A
	Q	WO 95/14079	May 26/95	PCT	Myocardial grafts and cellular compositions useful for same	N/A
	R	WO 99/49015	Sep 30/99	PCT	Cardiac-derived stem cells	N/A
	S	WO 00/06701	Feb 10/00	PCT	Improvement of cardiac function by mesenchymal stem cell transplantation	N/A
/MN/	T	WO 00/70021	Nov 23/00	PCT	Differentiated human embryoid cells and a method for producing them	N/A

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Form 1449 (modified) 37 C.F.R. §1.97 Information Disclosure Statement By Applicant  (Use Several Sheets if Necessary)
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Docket: 099/004P

U.S.S.N. 10/805,099

Title: Process for Making Transplantable Cardiomyocytes from Human Embryonic  
Stem Cells  
Inventors: Chunhui Xu, et al.

Filing Date: March 19, 2004

Group: 1632

## Foreign Patent or Published Foreign Patent Application

Examiner Initial	Ref.	Document No.	Publication Date	Jurisdiction	Title	Translation
/MN/ U	WO 00/78119	Dec 28/00	PCT	Cardiomyocytes with enhanced proliferative potential, and methods for preparing and using same		N/A
	V	WO 01/22978	Apr 5/01	PCT	Autologous marrow stem cell (MSC) transplantation for myocardial regeneration	N/A
	W	WO 01/51616	Jul 19/01	PCT	Techniques for growth and differentiation of human pluripotent stem cells	N/A
	X	WO 01/53465	Jul 26/01	PCT	Human embryoid body-derived cells	N/A
	Y	WO 01/68814	Sep 20/01	PCT	Multipotent cell and cardiomyocyte cell populations, and routes to and uses of same	N/A
	Z	WO 02/09650	Feb 7/02	PCT	Methods and compositions for the repair and/or regeneration of damaged myocardium	N/A
	AA	WO 02/13760	Feb 21/02	PCT	Methods and compositions for the repair and/or regeneration of damaged myocardium	N/A
	AB	WO 02/19893	Mar 14/02	PCT	Method for the improvement of cardiac function in a living subject after myocardial infarction via intramyocardial implantation of mammalian embryonic stem cells	N/A
	AC	WO 02/30206	Apr 18/02	PCT	Genetically altered mammalian embryonic stem cells, their living progeny, and their therapeutic application for improving cardiac function after myocardial infarction	N/A
	AD	WO 03/006950	Jan 23/03	PCT	Cells of the cardiomyocyte lineage produced from human pluripotent stem cells	N/A
/MN/	AE	WO 04/081205	Sep 23 2004	PCT	Differentiation of human embryonic stem cells to cardiomyocytes	N/A

## Other Documents

Examiner Initial	Ref.	Author, Title, Source, Date
/MN/	AF	Alsan et al., Regulation of avian cardiogenesis by Fgf8 signaling, Development, 129:1935 (2002)
	AG	Andree et al., BMP-2 induces expression of cardiac lineage markers and interferes with somite formation in chicken embryos, Mech. of Deve., 70:119 (1998)
	AH	Antin et al., Regulation of avian precardiac mesoderm development by insulin and insulin-like growth factors, J. Cell. Physiol. 168:42 (1996)
	AI	Arai et al., Murine cardiac progenitor cells require visceral embryonic endoderm and primitive streak for terminal differentiation, Dev. Dynamics 210:344 (1997)
	AJ	Barron et al., Requirement for BMP and FGF signaling during cardiogenic induction in non-precardiac mesoderm is specific, transient, and cooperative, Dev. Dynamics 218:383 (2000)
	AK	Bauwens et al., Development of perfusion fed bioreactor for embryonic stem cell-derived cardiomyocyte generation: oxygen-mediated enhancement of cardiomyocyte output, biotechnology and bioengineering 90 (4):452 (2005)
	AL	Behfar et al., Stem cell differentiation requires a paracrine pathway in the heart, FASEB J, 16:1558 (2002)
/MN/	AM	Claycomb et al., HL-1 cells: A cardiac muscle cell line that contracts and retains phenotypic characteristics of the adult cardiomyocyte, Proc. Natl. Acad. Sci. USA 95:2979 (1998)

Examiner	Date Considered
/Marcia Noble/	03/29/2007

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Form 1449 (modified) 37 C.F.R. §1.97 Information Disclosure Statement By Applicant  (Use Several Sheets if Necessary)	Docket: 099/004P  Title: Process for Making Transplantable Cardiomyocytes from Human Embryonic Stem Cells Inventors: Chunhui Xu, et al.  Filing Date: March 19, 2004	U.S.S.N. 10/805,099  Group: 1632
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### Other Documents

Examiner Initial	Ref.	Author, Title, Source, Date
/MN/	AN	Dang et al. Controlled, scalable embryonic stem cell differentiation culture, <i>Stem Cells</i> , 22:275 (2004)
	AO	Doevendans et al., Differentiation of cardiomyocytes in floating embryoid bodies is comparable to fetal cardiomyocytes, <i>J. Mol. Cell Cardiol</i> , 32:839 (2000)
	AP	Dubus et al., Contractile protein gene expression in serum-free cultured adult rat cardiac myocytes, <i>Pflugers Arch</i> , 423:455 (1993)
	AQ	Fukuda, Development of regenerative cardiomyocytes from mesenchymal stem cells for cardiovascular tissue engineering, <i>Artificial Organs</i> 25:187 (2001)
	AR	Gepstein, Derivation and Potential Applications of Human Embronic Stem Cells, <i>Circulation Research</i> , 91 (10):866 (2002)
	AS	Grepin et al., Enhanced cardiogenesis in embryonic stem cells overexpressing the GATA-4 transcription factor, <i>Development</i> 124:2387 (1997)
	AT	Gryschenco et al., Outwards currents in embryonic stem cell-derived cardiomyocytes, <i>Pflugers Arch</i> . 439:798 (2000)
	AU	Heng et al., Strategies for directing the differentiation of stem cells into the cardiomyogenic lineage in vitro, <i>Cardiovascular Research</i> , 62:34 (2004)
	AV	Itskovitz-Eldor et al., Differentiation of Human Embronic Stem Cells into Embryoid Bodies Comprising the Three Embryonic Germ Layers, <i>Mol. Med.</i> 6:88 (2000)
	AW	Johansson et al., Evidence for involvement of activin A and bone morphogenetic protein 4 in mammalian mesoderm and hematopoietic development, <i>Molecular and Cellular Biology</i> , 15(1):141 (1995)
	AX	Kawai et al., Efficient cardiomyogenic differentiation of embryonic stem cell by fibroblast growth factor 2 and bone morphogenetic protein 2, <i>Circ J</i> 68:691 (2004)
	AY	Kehat et al., Electromechanical integration of cardiomyocytes derived from human embryonic stem cells, <i>Nature Biotechnology</i> , 22(10):1282 (2004)
	AZ	Kehat et al., Abstract, Human embryonic stem cells can differentiate into cyocytes with structural and functional properties of cardiomyocytes, <i>J. Clin. Invest.</i> , 108:407 (2001)
	BA	Kehat et al., Long term high-resolution, Electrophysiological assessment of human embryonic stem cell derived cardiomyocytes: A novel in vitro model for the human heart, <i>Circulation</i> , 102(18 Suppl.II):II-4 (2000)
	BB	Kessler et al., Myoblast cell grafting into heart muscle: Cellular biology and potential applications, <i>Annu. Rev. Physiol.</i> 61:219 (1999)
	BC	Klug et al. Genetically selected cardiomyocytes from differentiating embryonic stem cells form stable intracardiac grafts, <i>J. Clin. Invest.</i> 98:216 (1996)
	BD	Koide et al., Atrial natriuretic peptide accelerates proliferation of chick embryonic cardiomyocytes in vitro, <i>Differentiation</i> 61:1 (1996)
	BE	Kolossov et al., Functional characteristics of ES cell-derived cardiac precursor cells identified by tissue-specific expression of the green fluorescent protein, <i>J. Cell Biol.</i> 143:2045 (1998)
	BF	Ladd et al., Regulation of avian cardiac myogenesis by activin/TGFB and bone morphogenetic proteins, <i>Dev. Biology</i> 204:407 (1998)
	BG	Lev et al., Differentiation pathways in human embryonic stem cell-derived cardiomyocytes, <i>Ann. N.Y. Acad. Sci.</i> 1047:50 (2005)
	BH	Liechty et al., Human mesenchymal stem cells engraft and demonstrate site-specific differentiation after in utero transplantation in sheep, <i>Nature Med.</i> 6:1282 (2000)
/MN/	BI	Li et al., Isolation of cardiomyocytes from human myocardium for primary cell culturing, <i>J. Tiss. Cult. Meth.</i> 15:147 (1993)

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(Use Several Sheets if Necessary)	Filing Date: March 19, 2004	Group: 1632

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/MN/	BJ	Lough et al., Combined BMP-2 and FGF-4, but neither factor alone, induces cardiogenesis in non-precardiac embryonic mesoderm, Dev. Biology 178:198 (1996)
	BK	Makino et al., Cardiomyocytes can be generated from marrow stromal cells in vitro, J. Clin. Invest. 103:697 (1999)
	BL	Maltsev et al., Embryonic stem cells differentiate in vitro into cardiomyocytes representing sinusnodal, atrial and ventricular cell types, Mechanisms Dev. 44:41 (1993)
	BM	Matsushita et al., Formation of cell junctions between grafted and host cardiomyocytes at the border zone of rat myocardial infarction, Circulation 100[suppl. II]: II-262 (1999)
	BN	Marvin et al., Inhibition of Wnt activity induces heart formation from posterior mesoderm, Genes Dev. 15:316 (2001)
	BO	McBurney et al., Control of muscle and neuronal differentiation in a cultured embryonal carcinoma cell line, Nature 299:165 (1982)
	BP	McDowell et al., Activin as a morphogen in Xenopus mesoderm induction, Seminars in Cell & Development Biology, 10:311 (1999)
	BQ	Menard et al., Transplantation of cardiac-committed mouse embryonic stem cells to infarcted sheep myocardium: preclinical study, Lancet 366:1005 (2005)
	BR	Messina et al., Isolation and expansion of adult cardiac stem cells from human and murine heart, 95:911 (2004)
	BS	Min et al., Transplantation of embryonic stem cells improves cardiac function in postinfarcted rats, J. Appl. Physiol. 92:288 (2002)
	BT	Monzen et al., Bone morphogenetic proteins induce cardiomyocyte differentiation through the mitogen-activated protein kinase kinase kinase kinase TAK1 and cardiac transcription factors CsxNkx-2.5 and GATA-4, Mol. Cell Biol. 19:7096 (1999)
	BU	Muller et al., Selection of ventricular-like cardiomyocytes from ES cells in vitro, FASEB J. 14:2540 (2000)
	BV	Mummery et al., Cardiomyocyte differentiation of mouse and human embryonic stem cells, J Anat., 200 (Pt 3):233 – 242, 2002
	BW	Mummery et al., Differentiation of human embryonic stem cells to cardiomyocytes: Role of coculture with visceral endoderm-like cells, Circulation, 107:2733 (2003)
	BX	Muslin et al., Well-defined growth factors promote cardiac development in axolotl mesodermal explants, Development 112:1095 (1991)
	BY	Narita et al., Cardiomyocyte differentiation by GATA-4-deficient embryonic stem cells, Development 124:3755 (1997)
	BZ	Olson et al., Molecular pathways controlling heart development, Science 272:671 (1996)
	CA	Odorico et al., Multilineage differentiation from human embryonic stem cell lines, Stem Cells, 19:193 (2001)
	CB	Oh et al. Cardiac progenitor cells from adult myocardium: Homing, differentiation, and fusion after infarction, PNAS 100(21): 12313 (2003)
	CO	O'Shea, Embryonic Stem cell models of development, Anatomical Record, 257 (1):32 (1999)
	CC	Qin et al., Gene transfer of transforming growth factor-B1 prolongs murine cardiac allograft survival by inhibiting cell-mediated immunity, Human Gene Therapy 7:1981 (1996)
	CD	Reubinoff et al., Embryonic stem cell line from human blastocysts: somatic differentiation in vitro, Nature Biotech. 18:399 (2000)
/MN/	CE	Satin et al., Mechanism of spontaneous excitability in human embryonic stem cell derived cardiomyocytes, J Physiol 559(2):479 (2004)

Examiner	Date Considered
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 PTO-1449 — Page 4

Form 1449 (modified) 37 C.F.R. §1.97 Information Disclosure Statement By Applicant  (Use Several Sheets if Necessary)	Docket: 099/004P  Title: Process for Making Transplantable Cardiomyocytes from Human Embryonic Stem Cells Inventors: Chunhui Xu, et al.  Filing Date: March 19, 2004	U.S.S.N. 10/805,099  Group: 1632
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/MN/	CF	Scalia et al., Regulation of the Akt/Glycogen synthase kinase-3 axis by insulin-like growth factor-II via activation of the human insulin receptor isoform-A, <i>J. Cell. Biochem.</i> 82:610 (2001)
	CG	Schlange et al., BMP2 is required for early heart development during a distinct time period, <i>Mechanisms of Development</i> , 91:259 (2000)
	CH	Schneider et al., Wnt antagonism initiates cardiogenesis in <i>Xenopus laevis</i> , <i>Genes Dev.</i> 15:304 (2001)
	CI	Schuldiner et al., Effects of eight growth factors on the differentiation of cells derived from human embryonic stem cells, <i>PNAS</i> 97:11307 (2000)
	CL	Schultheiss et al., Induction of avian cardiac myogenesis by anterior endoderm, <i>Development</i> 121:4203 (1995)
	CJ	Schultheiss et al., A role for bone morphogenetic proteins in the induction of cardiac myogenesis, <i>Genes &amp; Dev.</i> 11:451 (1997)
	CK	Shambrott et al., Derivation of pluripotent stem cells from cultured human primordial germ cells, <i>Proc. Natl. Acad. Sci. USA</i> 95:13726 (1998)
	CM	Shi et al., BMP signaling is required for heart formation in vertebrates, <i>Dev. Biol.</i> 224:226 (2000)
	CN	Skerjane, et al., Myocyte enhancer factor 2C and Nkx2-5 up-regulate each other's expression and initiate cardiomyogenesis in P19 cells, <i>J. Biol. Chem.</i> 273:34904 (1998)
	CP	Sugi et al., Activin-A and FGF-2 mimic the inductive effects of anterior endoderm on terminal cardiac myogenesis in vitro, <i>Dev. Biology</i> 168:567 (1995)
	CQ	Symes et al., Morphological differences in <i>Xenopus</i> embryonic mesodermal cells are specified as and early response to distinct threshold concentrations of activin, <i>Development</i> 120:2339 (1994)
	CR	Thomson et al., Embryonic stem cell lines derived from human blastocysts, <i>Science</i> 282:1145 (1998)
	CS	Velez et al., Modulation of contractile protein troponin-T in chick myocardial cells by basic fibroblast growth factor and platelet-derived growth factor during development, <i>J. Cardiovascular Pharmacology</i> 24:906 (1994)
	CT	Volz et al., Longevity of adult ventricular rat heart muscle cells in serum-free primary culture, <i>J. Mol. Cell Cardiol.</i> 23:161 (1991)
	CU	Walters et al., Bone morphogenetic protein function is required for terminal differentiation of the heart but not for early expression of cardiac marker genes, <i>Mechanisms of Development</i> , 100:263 (2001)
	CV	Wobus et al., In vitro cellular models for cardiac development and pharmacotoxicology, <i>Toxic. in Vitro</i> 9:477 (1995)
	CW	Wobus et al., Development of cardiomyocytes expressing cardiac-specific genes, action potentials, and ionic channels during embryonic stem cell-derived cardiogenesis, <i>Ann. N.Y. Acad. Sci.</i> 752:460 (1995)
	CX	Wobus et al., Retinoic acid accelerates embryonic stem cell-derived cardiac differentiation and enhances development of ventricular cardiomyocytes, <i>J. Mol. Cell Cardiol.</i> 29:1525 (1997)
	CY	Xu et al., Feeder-free growth of undifferentiated human embryonic stem cells, 19 (10): 971 (2001)
	CZ	Xu et al., Characterization and enrichment of cardiomyocytes derived from human embryonic stem cells, <i>Circulation Research</i> , 91 (6): 501 (2002)
	DA	Xu et al., Specific arrest of cardiogenesis in cultured embryonic stem cells lacking Cripto-1, <i>Dev Biol.</i> 196:237 (1998)
	DB	Yatskiewych et al., Induction of cardiac myogenesis in avian pregastrula epiblast: the role of the hypoblast and activin, <i>Development</i> , 124:2561 (1997)
/MN/	DC	Zandstra et al., Scalable production of embryonic stem cell-derived cardiomyocytes, <i>Tissue Engineering</i> , 9(4):767 (2003)

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/Marcia Noble/	03/29/2007

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<b>Form 1449 (modified)</b> <b>37 C.F.R. §1.97</b> <b>Information Disclosure</b> <b>Statement By Applicant</b>  (Use Several Sheets if Necessary)	<b>Docket: 099/004P</b> <b>U.S.S.N. 10/805,099</b>  <b>Title: Process for Making Transplantable Cardiomyocytes from Human Embryonic Stem Cells</b> <b>Inventors: Chunhui Xu, et al.</b>  <b>Filing Date: March 19, 2004</b> <b>Group: 1632</b>
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### Other Documents

Examiner Initial	Ref.	Author, Title, Source, Date
/MN/	DD	Zhu et al., Evidence that fibroblast growth factors 1 and 4 participate in regulation of cardiogenesis, Dev. Dynamics 207:429 (1996)
/MN/	DE	Zingg et al., Genetic and epigenetic aspects of DNA methylation on genome expression, evolution, mutation and carcinogenesis, Carcinogenesis 18:869 (1997)

  
**Marcia  
Noble**

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Noble  
on 2009-12-22 13:26:37  
US  
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12/22/2009

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Marcia S. Noble	/Marcia Noble/ 03/29/2007

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